36. (New) The method of Claim 14, wherein the neurotrophin is nerve growth factor, neurotrophin-3, neurotrophin 4/5 or brain-derived neurotrophic factor.

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37. (New) The method of Claim 14 wherein the biologically active fragment is a peptide comprising amino acid sequence lysine-glycine-alanine.

38. (New) The method of Claim 37 wherein the peptide consists of SEQ ID NO:4, SEQ ID NO:9 or SEQ ID NO:10.

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REMARKS

Claims 11 and 15 have been canceled. Claims 10 and 14 have been amended. Claims 33-38 have been added.

Note that the peptides consisting of SEQ ID NO: 4, SEQ ID NO: 9 or SEQ ID NO: 10 are all peptides comprising KGA.

Rejection of Claims 10 and 14 Under 35 U.S.C. § 112, First Paragraph (Item 5 of Office Action)

Claims 10 and 14 have been rejected under 35 U.S.C. § 112, first paragraph, as "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." The Examiner explains further, "Claims which recite pseudo-ligands that are defined as any substance which mimics a neurotrophin's ability to bind to the p75 nerve growth factor receptor fail to meet the description requirement of U.S.C. § 112, first paragraph."

Claims 10 and 14 have been amended to eliminate the term "pseudo-ligand."

Rejection of Claims 10 and 14 Under 35 U.S.C. § 112, First Paragraph (Item 6 of Office Action)

Claims 10 and 14 have been rejected under 35 U.S.C. § 112, first paragraph, "because the specification, while being enabling for methods employing substances such as neurotrophin or a

biologically active fragment thereof, does not reasonably provide enablement for methods using pseudo-ligands."

Claims 10 and 14 have been amended to eliminate the term "pseudo-ligand."

Rejection of Claims 10-11 and 14-15 Under 35 U.S.C. § 102(b) (Item 8 of Office Action)

Claims 10-11 and 14-15 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Reams (W.M. Reams, *J. Invest. Dermatol. 49*:552-558, 1967). Claims 11 and 15 have been canceled.

The Reams paper reports studies performed on black mice, the untreated mice of a PET (Pigmented Extraepidermal Tissue) genetic strain having dark skin and black fur. Ten days after daily consecutive treatments with nerve growth factor injected at a site under the skin, there were three different zones of reaction in concentric rings at the site of injection. At the center was a region of dense, small, normally structured black hairs. In a ring outside of this region, was a second region with small, black, curly hairs and small, sparsely scattered hairs. The author notes that in this second region, "Integumentary melanocytes were frequently lacking – especially in the region of the curly hairs." Thus, it appears that the pigment forming cells normally present in the skin had become more scarce. In a third region forming a ring outside of the first two regions was a region of white hairs and gray hairs of normal length and structure.

In animals that have as their normal condition dark skin and black fur, it is incorrect to conclude that nerve growth factor had the effect of "maintaining or inducing hair color" or "inducing or maintaining skin color" when there were mixed results, among them the loss of color in the hairs and the decrease in density of melanocytes in the skin. There is no indication that hair color or skin color was induced over the normal condition in the mice used in this experiment. One of ordinary skill in the art would not recognize the procedure followed by Reams as a method to maintain hair color or skin color, when the result of the procedure included depigmentation, the very opposite of the desired outcome. Thus, Reams does not teach all the elements of the rejected claims, and in fact, teaches away from the rejected claims.

## CONCLUSION

The Examiner is respectfully requested to consider the above amendments and remarks. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

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MARKED UP VERSION OF AMENDMENTS

Claim Amendments Under 37 C.F.R. § 1.121(c)(1)(ii)

10. (Amended) A method of maintaining or inducing hair color in a [vertebrate] mammal, said method comprising inhibiting p75 nerve growth factor receptor-mediated apoptosis in epidermal melanocytes wherein the apoptosis is inhibited by contacting the melanocytes with [a substance, wherein the substance is] a neurotrophin[,] or a biologically active fragment thereof [or a nerve growth factor pseudo-ligand] that binds to the p75 nerve growth factor receptor expressed on melanocytes.

14. (Amended) A method of inducing or maintaining skin color in a vertebrate comprising inhibiting p75 nerve growth factor receptor-mediated apoptosis in epidermal melanocytes wherein apoptosis is inhibited by contacting the melanocytes with a [substance, wherein the substance is a] neurotrophin[,] or a biologically active fragment thereof [or the pseudo-ligand is a nerve growth factor pseudo-ligand] that binds to the p75 nerve growth factor receptor expressed on melanocytes.